REMARKS/ARGUMENTS

Claims

Of claims 1-39 which were contained in the original application, claims 6-39 have been withdrawn from further consideration, as being drawn to a non-elected invention. Applicants reaffirm the election of claims 1-5, with traverse. Of claims 1-5, claims 1 and 2 are now cancelled and claims 3-5 remain under consideration. New claims 40 and 41 have been added to this application. No new matter has been introduced as a result of these new claims. Applicants reserve the right to present claims 6-39 in a divisional application.

Claims 3 and 4 are currently amended to incorporate the language "*consisting essentially of*". In addition, claims 3-5 have been amended to incorporate the language "a chromosomal gene of an Epstein-Barr virus nucleic acid molecule, under stringent conditions, which encodes a conserved EBNA2 region of the Epstein-Barr virus genome ..." Antecedent basis for these amendments can be found in paragraphs 24, 49, 69 of the present application. These are not narrowing amendments. No new matter is being introduced as a result of these amendments. New claims 40 and 41 have been added to this application. Antecedent basis for these new claims may be found in paragraphs 20 and 55 of the pending application.

Filing Receipt

Applicants previously requested a corrected filing receipt to correct the second inventor's name to read "Pamela A. Groen" on the filing receipt and issue a corrected filing receipt reflecting that correction. In addition, Applicants would like to have the Docket number 0010872/0482274 added to future correspondence. Applicants appreciate Examiner's help in these matters.

Specification

The Examiner has indicated that in Table III in the disclosure, the length of the primer of SEQ. ID. NO. 1 is incorrectly written as 20. The length has now been corrected to read 18 bases.

Rejections Under 35 U.S.C. §112, first paragraph

Claims 1 and 3-5 have been rejected under 35 USC §112, first paragraph. The Examiner maintains that the specification, while being enabling for a probe or a pair of primers consisting of SEQ. ID. Nos. 1 and 2, which are able to specifically hybridize and detect Epstein–Barr virus (EBV) under a stringent hybridization conditions, does not reasonably provide enablement for having any or all nucleic acid sequences using a probe having as low as 80% homology or any or all pairs of primers, comprising or consisting essentially of a pair of nucleic acid sequences, wherein the pair of nucleotide sequences have as low as 95% homology to SEQ. ID No. 1 and 2 or a base nucleic acid change of SEQ. ID.

Nos. 1 and 2, which is specifically able to detect EBV. The Examiner argues that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Applicants respectfully traverse this rejection.

The Examiner argues that the test of scope for enablement is whether one skilled in the art could make or use the invention from the disclosures in the application coupled with information known in the art, without undue experimentation. Applicants respectfully submit that the specification does provide adequate direction to those skilled in the art and that the disclosure would not require undue experimentation. Furthermore, the claims have now been amended to more clearly set forth the invention as an isolated and purified oligonucleotide primer pair for enzymatic amplification of Epstein-Barr virus DNA. The primer pair comprises a pair of nucleic acid sequences that complement and specifically hybridize to a chromosomal gene of an Epstein-Barr virus nucleic acid molecule under stringent conditions, which encodes a conserved EBNA2 region of the Epstein-Barr virus genome. The pair of nucleic acid sequences is at least 95% homologous to sequences selected from the group consisting of: (a) the oligonucleotide pairs of SEQ. ID. NO. 1 and SEQ. ID NO. 2; and (b) the oligonucleotide pair of SEQ. ID. NO. 5 and SEQ. ID. NO. 6.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with the information known in the art without undue experimentation. Experimentation is acceptable, even if some degree of repetition will likely to be necessary to achieve the desired result. Thus, in *In re Wands* 858 F.2d. 731 (Fed. Cir. 1988), where the claim required IgM antibodies with high affinity for the

hepatitis antigen, only a fraction of the screen antibodies were IgM and only a fraction of those had the minimum level of affinity. However, the Federal Circuit stated that the experiment was not screening a single hybridoma, rather screening a whole library of hybridomas. It was likely that in any given hybridoma library, at least one member would secrete antibodies with the desired characteristics.

This principle was extended to transgenic fish in *Ex parte Chen* (61 USPQ2d 1025 (Bd. Pat. Appeals Interf. 2000) (unpublished)) where the success rate was low and only 20 of 1746 attempts (1%) to achieve integration of the transgene into the fish genome were successful. The Board declared that "the numbers emphasized by the Examiner would reasonably appear to reflect the need for repetitive procedure, rather than undue experimentation." Thus, the present art typically engages in such repetitive procedures and, even if it may be complex, such experimentation is not necessarily undue.

In re Wands suggests that the following factors should be considered in determining whether a disclosure requires under experimentation:

1) *The nature of the invention*. Applicants submit that the nature of the invention lends itself to the fact that the amount of experimentation required to perform the broadly claimed methods is not undue. This factor supports the Applicants' contention that the disclosure does not require undue experimentation since repetitive testing procedures are all that is required to determine oligonucleotide primer pairs that will complement and specifically hybridize to a chromosomal gene of an Epstein-Barr virus nucleic acid molecule under stringent conditions.

2) *The breadth of the claims*. Although the Examiner contends that the claims are broad in that the oligonucleotide can be more than the size of SEQ. ID Nos. 1 and 2, the claim is not overly broad because Applicants have disclosed the sequence that the oligonucleotides must be taken from as well as the concise mechanism of action that the claims of the present application require – i.e., the claims require an oligonucleotide primer pair for enzymatic amplification of Epstein-Barr virus DNA, and the pair of nucleic acid sequences has been defined as sequences 95% homologous to sequences selected from the group consisting of (a) the oligonucleotide pairs of SEQ. ID. NO. 1 and SEQ. ID NO. 2; and (b) the oligonucleotide pair of SEQ. ID. NO. 5 and SEQ. ID. NO. 6. Therefore, the claims are not as broad as indicated by the Examiner. They cover the true scope of the present invention and embodiments falling within those claims are easily determined by those skilled in the art by commonly known procedures.

3) *The unpredictability of the art and the state of the prior art*. The Examiner appears to have taken the stance that oligonucleotides as a whole are unpredictable and it would be difficult to provide any nucleotide sequence comprising 95% homology of SEQ. ID. Nos. 1 and/or 2 (see amended claims 3-5) that would be able to specifically hybridize EBV because of the size of the probe and the content of the nucleotide sequences would use different conditions for a specific hybridization. Because of the unpredictability of living processes, generic biological claims inherently must cover inoperative members of the class. This is not fatal to the claim if a person skilled in the art can without undue

experimantation, recognize which species are operative and which are not, especially if functional limitations are used to exclude inoperative members. In the present case, inoperative members are specifically excluded through the functional limitations that the oligonucleotide primer pairs must consist essentially of a pair of nucleic acid sequences which complement and specifically hybridize to a chromosomal gene of an Epstein-Barr virus nucleic acid molecule under stringent conditions. The oligonucleotide pair of nucleic acid sequences must also be at least 95% homologous to sequences selected from the group consisting of (a) the oligonucleotide pairs of SEQ. ID. NO. 1 and SEQ. ID NO. 2 and (b) the oligonucleotide pair of SEQ. ID. NO. 5 and SEQ. ID. NO. 6. Thus, functional limitations are used to exclude inoperative members of the class and subclass.

4) *Working examples and guidance in the specification*. The Examiner seems to indicate that it is necessary to show working examples comparing **all** possible sequences. Examples are not necessary to satisfy the enablement requirement of 35 USC §112, first paragraph. A patent applicant is not required to predict every possible variation, improvement or commercial embodiment of his invention. (*Zoltek Corp. v. United States*, 48 Fed. Cl. 290; 57 U.S.P.Q.2D (BNA) 1257) Tables 1-5 of the present application do provide specific data and examples showing how one skilled in the art could utilize and practice this invention. Table 3 and paragraph 0128 provide examples of primers and/or primer pairs that may be used to practice the invention. Furthermore, paragraph 0127 describes the assay procedure in particular detail, including a description of the EBV genome

and the unique domains of the gene. Thus, the specification does provide detailed examples for how to make and use this invention.

5) *Quantity of experimentation.* While it is true that the present invention would require some experimentation to determine which specific oligonucleotides could be used as primers to amplify particular regions of the Epstein-Barr virus to be detected in a clinical specimen, the level of experimentation required is not high relative to the level of skill in the art and complexity of the art. Applicants have provided working examples that show the use of different sequences for the diagnosis and quantitation of an Epstein-Barr virus infection. An extended period of experimentation is not undue if the skilled artisan is given sufficient direction or guidance. "The test is not merely quantitative since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 8 USPQ2d at 1404 (CCPA 1076). The time and expense are merely factors in this consideration and are not the controlling factors.

In the present invention, the Examiner has interpreted "undue experimentation" in a way that would effectively render it impossible to obtain a generic claim in any chemical or biological art. This approach is clearly erroneous, as explained by *In re Angstadt* 537 F.2d. 498 (C.C.P.A. 1976). In *In re Angstadt*, the court stated that to require such a complete disclosure would apparently necessitate a patent application or applications with "thousands"

of examples. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous oligonucleotide primer pair which could be used to amplify particular regions of the Epstein-Barr virus for detection in a specimen.

Thus, is respectfully submitted that the present specification fully meets the requirements of 35 U.S.C. §112, first paragraph, and withdrawal of these rejections is respectfully requested.

Rejections Under 35 U.S.C. 102(b)

The Examiner has rejected claims 1 and 2 under 35 USC §102(b) as being anticipated by Sorge, *et al.* (WO95/16028A1). In making this rejection, the Examiner has pointed out that SEQ. ID NO:29 of the Sorge *et al.*, reference is 100% homologous to SEQ. ID NO:2 in the present application. Claims 1 and 2 have now been cancelled. Therefore, the Examiner's rejection of claims 1 and 2 is moot.

In addition, while claims 3-5 also require SEQ. ID. NO. 2, these claims differ from claims 1 and 2 in that SEQ. ID. NO. 2 is claimed as half of a *primer pair*, the other half being SEQ. ID. NO. 1. Sorge et al. does not disclose (or suggest) the claimed primer pair. Thus,

claims 3-5 do not anticipate Sorge et al. since claims 3-5 utilize SEQ. ID. NO. 2 as half of a *primer pair*.

In light of all the foregoing amendments and remarks, it is submitted that the claims of the present application, as amended herein, are now and form for allowance. Accordingly, early reconsideration and allowance of the claims, as currently pending, are solicited.

Respectfully submitted,

Pamela A. Groen, *et al.*

"Express Mail" Mailing Label Number:
EV 311437585 US

Date of Deposit: 2-5-04

I hereby certify that this paper or fee is being deposited in the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and is addressed to Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

Typed or Printed Name of Person Signing

2/5/04

Karlyn A. Schnapp
Registration No. 45,558
Telephone (513) 651-6865
FROST BROWN TODD LLC
2200 PNC Center
201 East Fifth Street
Cincinnati, Ohio 45202-4182

CinLibrary/1348239.1